

**WHAT IS CLAIMED IS**

1. A method of detecting PDZ polypeptide binding to an alpha adrenergic receptor, comprising:
  - a) combining a labeled polypeptide containing an alpha adrenergic receptor C-terminal PL sequence with a PDZ polypeptide *in vitro*, and
    - b) detecting binding between the PDZ polypeptide and the alpha adrenergic receptor polypeptide
2. The method of claim 1 wherein the PL polypeptide is a biotinylated peptide.
3. The method of claim 1 wherein the PL polypeptide is a fluorescence labeled peptide.
4. The method of claim 1 wherein the PL polypeptide is an epitope tagged protein expressed in a host cell.
5. A method of determining whether a test compound is a modulator of binding between a PDZ polypeptide and an alpha adrenergic PL polypeptide, comprising:
  - (a) contacting under suitable binding conditions (i) a PDZ polypeptide, and (ii) a PL peptide, wherein
    - the PL peptide comprises a C-terminal sequence of the PL polypeptide,
    - the PDZ polypeptide and the PL peptide are a binding pair as specified in

20 Table 8; and

contacting is performed in the presence of the test compound; and

(b) detecting formation of a complex between the PDZ-domain polypeptide and the PL peptide, wherein

(i) presence of the complex at a level that is statistically

25 significantly higher in the presence of the test compound than in the absence of test compound is an indication that the test compound is an agonist, and

(ii) presence of the complex at a level that is statistically significantly lower in the presence of the test compound than in the absence of test compound is an indication that the test compound is an antagonist.

6. The method of claim 5, wherein the modulator is a peptide.
7. A modulator of binding between a specific PDZ polypeptide and an alpha adrenergic receptor PL polypeptide, wherein the modulator is
  - (a) a peptide comprising at least 3 residues of a C-terminal sequence demonstrated to bind the target PDZ polypeptide; or
  - (b) a peptide mimetic of the peptide of section (a); or
  - (c) a small molecule having similar functional activity as the peptide of section (a) with respect to the PDZ polypeptide and PL polypeptide binding pair.
8. The modulator of claim 7 that modulates a specific interaction listed in Table 8.
9. The modulator of claim 7 that is an agonist.
10. The modulator of claim 7 that is an antagonist.
11. A pharmaceutical composition comprising a modulator of claim 7.
12. A method of treating a disorder from Table 9, comprising administering a therapeutically effective amount of a modulator of claim 7, wherein the PDZ polypeptide and the alpha adrenergic receptor PL polypeptide are a binding pair as specified in Table 8.